MICROCOCCUS POISONING. By Alex. Ogston, M.D.,

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(*Continued from* vol. xvi. *p.* 567).

Sapræmia.

(σαπρός, putrid; αἷμα, blood.)

This term was first used by Dr. Matthews Duncan[1] to signify "mere poisoning by the chemical products of putrefaction," and concerning it he says:—

"Sapræmia, or simple putrid intoxication—poisoning not by an organism multiplying in the blood, but by the passing into it of the chemical products of putrid decomposition—is one upon which much light has been recently thrown, and with the most beneficial results in practice. Like the other forms of the so-called puerperal fever, this I shall treat as a separate entity, and it frequently is so. But it may be combined with the traumatic fever of inflammation, and it is especially liable to be combined with septicæmia and pyæmia. Indeed, it has long been, and still is, the habit to speak of septicæmia and pyæmia as diseases of putrefaction, but this is a mistake. Putridity of the discharges is not an essential part of these diseases at all, though it often accompanies them. The organisms which cause septicæmia and pyæmia probably take no part in putrefaction. They live in the discharges, and are conveyed or pass into the blood, where they multiply indefinitely. The organisms which cause putrefaction, whether the *Bacterium termo*, or others in addition, may pass into the blood with the putrid fluids to produce sapræmia, but they do not survive, far less grow therein.

"We have then, in sapræmia, when uncomplicated, a very simple problem. Putrid ichor is absorbed, or flows through the uterine sinuses, or otherwise, into the circulation. Its poisonous constituents are eliminated rapidly from the blood, for if the supply is stopped the sapræmic phenomena quickly disappear.

"When once in the blood it does not increase in it, ferment-like, independently of any other supply. Sapræmia is kept up by a continuous supply of the poison. It disappears when the supply from without is stopped. To stop the supply is the problem of the cure."

In all that concerns sapræmia, this description is probably perfect. It is beyond doubt that there are organisms (saprophytes) that produce *common putridity*, and others that cause

[1] "Puerperal Fever," *Lancet*, 1880, vol. ii. p. 684.

decompositions that are not putridity. To the former belong most, if not all, forms of bacterium, some bacilli, and some spirilla. To the latter belong some bacilli and some micrococci. If micrococcus be introduced into a fluid and there cultivated, it produces no offensive stench; its ptomaïnes are not those of putridity. In most acute abscesses, where it is found in abundance, no bad odour is detectable,[1] and if the contents of an abscess, or a fluid where organisms have been growing, be found to present a putrid smell, we are absolutely certain to detect in it numerous organisms that possess either the sausage shape of the bacterium or the rod form of the bacillus.

These sapro-micro-organisms produce disease in a manner peculiarly their own. Koch[2] thus describes their mode of action:—

"Five drops are enough to kill a mouse within a short time. Immediately after they have been injected, distinct morbid symptoms are observable in the animal. It becomes restless and runs much about, yet showing great weakness and unsteadiness of movement, ceases to eat, the respiration becomes irregular and slow, and death ensues in four to eight hours. In such animals the connective tissue of the injection site still contains the greater part of the injected fluid in the same condition as when it was injected.

"It shows the same numbers of various organisms mixed through each other, just as the microscope showed prior to injection; but there is no reaction in the neighbourhood, the viscera are unaltered, the blood taken from the right auricle produces no result if inoculated on another mouse, and organisms are found neither in the blood nor the internal organs."

The animal has been poisoned by the ptomaïnes—*i.e.*, the gases and liquids of the sapro-micro-organisms.

In man we find this sapræmia in various forms and degrees. The slightest form is the sickness and nausea produced by a bad smell, which is but a ptomaïne of putridity, and which has been known to produce serious symptoms without the possibility of entrance into the body of the micro-organisms that generated it.

Its usual and most marked manifestations are in the sapræmia of childbed, which Matthews Duncan has described, and in

[1] My endeavours to ascertain the kind and properties of the ptomaïnes of micrococcus have hitherto failed.

[2] *Wundinfectionskrankheiten*, p. 40.

fœtid abscesses such as those in or near the abdominal cavity—in the former case it may exist alone, in the latter its symptoms are mixed with those of septicæmia.

Where pure, as after childbed, its symptoms are the rising temperature, the hot skin striving by perspiration to throw off something that the system is resenting, the full pulse, the flushed face, the headache, and the occasional tendency to gastro-intestinal derangements. We see, in fact, that the system is poisoned, and the fœtid lochiæ, with probably putrefying clots, are evidently the pool of poison that is causing the evil. We wash out vagina and uterus, or it may be that we merely set our patient erect for a few moments and allow the fœtid clots and contents of the vagina and uterus to escape, and our disease is gone, defevrescence is the work of but a few hours, and the patient is cured. It is a poisoning, not an infection. In the blood we find a few organisms of the bacterium shape, the urine shows a number of long organisms with the characters of bacillus, but anything like a blood disease does not exist, there is but an intoxication.

Where complicated with septicæmia, as in most cases of fœtid abscess, the symptoms are a mixture of the two diseases, but the great alleviation, the improved colour, the diminished perspiration, the relief of the aching or oppressed head, and the return of the appetite that follow the issue of the stinking pus, point to the sapræmia induced by it being a condition *per se*, and the patient seems on the way to convalescence and health when it has been removed. Very often, however, the symptoms of septicæmia, that were little noticed in the presence of those of sapræmia, gradually come to the front, the improvement may be but temporary, and the patient may die after all.

In sapræmia, whether natural or produced experimentally, the sapro-micro-organisms that enter the blood are evidently too weak to overcome its vitality, for they do not show much evidence of being alive; they do not survive and cause putrefaction in the cavities or fluids, normal or pathological, into which it may convey them; they are probably consumed by the leucocytes, or in some other manner, for the urine in this disease, although it usually contains forms of bacilli alive and growing, that have passed into the system coincidently with the sapro-micro-organ-

isms, shows no trace of putrefaction nor of the forms of bacteria that produce it.

The sapro-micro-organisms are probably enfeebled or killed through their removal from the oxygen of the air, which is necessary for the full exhibition of their decomposing energies. I have already pointed out that bacteria grow best on the surfaces of liquids, where they form thick turfs in contact with the air, while at the bottom of the fluid, in deep jars, they are either dead or comparatively inactive. In such a state they are found in the blood in sapræmia, and are doubtless killed where the individual is in any save the most enfeebled condition, although the early onset of decomposition, commencing ere life is extinct, that we find in those who die from septic processes, as well as the fact that when they are injected into a very weakly and ailing animal, such as one dying of diarrhœa or other enfeebling disease, they may be found alive and growing in the blood at the moment of death, point to the probability of the entrance into and growth within the system of sapro-micro-organisms even before life has become extinct in all forms of fatal enfeebling disease.

Septicæmia, Pyæmia, and Septico-Pyæmia.

It will conduce to clearness and brevity at once to state that every fact that I have been able to observe regarding these diseases points to their being one and the same, and to their sole and invariable cause being *micrococcus poisoning.*

Micrococcus is met with in two distinct forms, chains and groups. They are often found together, yet the two are different, and the chain form does not pass into the grouped form, nor the grouped into the chain form. Throughout this paper the term *micrococcus* is used as embracing both forms; the chain coccus is often called *streptococcus* (Billroth), and I shall call the grouped form *staphylococcus* (from σταφυλή, a bunch of grapes).

Micrococcus, which, when limited in its extent and activity, causes acute suppurative inflammation (phlegmon), produces, when more extensive and intense in its action on the human system, the most virulent forms of septicæmia and pyæmia, as well as many forms intermediate between the two extremes.

The connection between suppuration and blood-poisoning is

no new idea; the very name *pyæmia* was conferred as implying the relationship; and the title of "purulent infection," though little used in English or German literature, is still the favoured term for the disease among the French clinicians. Nor is the idea of septico-pyæmia being equivalent to micrococcus-poisoning new, it has constantly been cropping up in various forms.[1]

Although at first it be somewhat repugnant to existing notions to consider acute inflammation but a slighter form of pyæmia, very little reflection will show that the statement is by no means a strange one. The common acute abscesses with which we are all so familiar are attended with febrile conditions not very unlike the fever of blood-poisoning, and the circumstances under which they occur, such, for instance, as in women shortly after childbed, are the very times when we also meet with the graver disease. Not only so, but acute inflammation, such as pneumonia, are very apt to end in blood-poisoning, and in the old and enfeebled, where this is naturally most usual, a separate clinical form where this is the rule has been described and rendered classical by Trousseau.[2] Acute inflammations of the peritoneum are closely connected with septicæmia, and acute suppurative inflammations of joints, as in urethral rheumatism, bring us a step nearer to pure blood-poisoning. Between an acute inflammation (whitlow) and a poisoned wound of the hand, there is no possibility of drawing a valid distinction, for not only do intermediate forms occur, but the one usually or frequently passes into the other. There is in reality no distinction between the erysipelatous blush surrounding an acute abscess in its angriest stage, the erysipelatoid infiltration that is common around the wounds of the septicæmic, and the phlegmonous erysipelas that is so often fatal from blood-poisoning. Acute suppurative inflammations of the arachnoid and pleura never occur save as part of a process of blood-poisoning; a suppurating ear needs but to extend itself to the bone and the lateral sinus (or brain), and, with no other change than that of site, has become a fatal septicæmic malady. Suppurations under the

[1] Cocco-bacteria septica, by Billroth, 1874; also Cocco-bacteria septica, by Billroth and Ehrlich, 1877, *Arch. f. Klin. Chir.*, vol. xx. p. 403; and elsewhere.

[2] *Clinique Médicale*, ed. 2, vol. i. p. 747.

scalp and in the diploë are dreaded chiefly owing to their intimate connection with septicæmic conditions; parotid abscess and acute suppurations in the glands of the neck are also almost synonymous with pyæmia. A quinsy runs its course with feverish symptoms that are of the same nature; necrosis of the jaws is always accompanied by septicæmia, as are also all acute suppurations of the thyroid gland. All acute abscesses about the thorax and abdomen, such as hepatic abscess, abscesses of the abdominal wall and around the cæcum, are of the septicæmic type; splenic and hepatic abscesses, renal abscesses, and miliary abscesses in these viscera and the heart, are all common conditions in pyæmia. Abscesses in the glands of the extremities, and among their soft parts, are always connected with septic or erysipelatous processes; while to name acute suppurative inflammations in bones or joints is but to name maladies whose whole appearance is that of blood-poisoning. It would be hard to find an acute suppuration anywhere where general symptoms of blood-poisoning may not be a prominent feature.

Since at all hands evidence is abundant that acute suppurative inflammation is closely allied to blood-poisoning, so closely that in any given case we have only to imagine it indefinitely increased to see that it must eventuate in the latter disease, the fact that nature shows so great a difference between the milder and the graver forms must not be allowed to blind us into the rejection of what can, I think, be shown to be an indubitable truth, and capable of being in all points rationally explained. There is nothing surprising or unexampled in mild cases of disease of the bacteric (zymotic) type, being very unlike their severe forms, and as examples may be quoted the instances of a mild attack of typhoid fever where a little feverishness and diarrhœa is almost all that is observed, and the virulent forms of the same where the patient may be even struck down comatose, like one in apoplexy, and die in stupor ere any of the usual appearances occur; or a mild attack of vesicular smallpox, as compared with a bad hæmorrhagic case where death occurs ere the eruption appears. It must be admitted that the difference between acute suppurative inflammation and septicæmia is not an unparalleled phenomenon, if it be the case that they are forms of one and the same disease.

Already, in an earlier part of this report, the theory has been developed that what we call inflammation is but a form of reaction, a perversion of the process of growth, which the tissues and the structures of the body present when injured by anything capable of damaging them, each irritating cause having its own specific reaction recognisable by the form of inflammation it presents, and that the characteristic reaction of micrococcus is acute suppurative inflammation (phlegmon).

I have also suggested that the term septicæmia is a misleading one, as in no case is the blood the focus of disease, but that this is to be found in the tissues, whence the ptomaïnes of the disease pass into the circulation to act as poisons or intoxicants, and separate individuals or small groups of the micro-organisms are conveyed by this fluid into other situations so as to reproduce among other tissues the disease of the parent focus. The term micrococcus poisoning, which does not include the idea of an essential blood-disease, would be in some respects a more suitable name than pyæmia or septicæmia. But to designate the more severe forms of micrococcus poisoning, and the conditions in which we infer from the symptoms that the system generally is becoming poisoned, I shall still retain the term septicæmia as a name, although refusing to agree with the belief that the condition implied by it really is an infection of the blood *per se.* Where the term septicæmia would mislead, the word "ptomaïne-poisoning" will be made use of.

Phlegmon or Acute Suppurative Inflammation.

The most ready means of studying this condition is to observe the results of injecting, into the tissues of animals, micrococcus as it exists free from admixture of any other micro-organism, in the pus of an acute abscess. Although micrococcus is perhaps the greatest scourge that afflicts the human race, it is by no means so pernicious to animals when injected, and some species are considerably less easily affected by it than others. Guinea-pigs are, I think, decidedly less sensitive than mice.

If two minims of the pus be injected under the skin of a mouse's back, the animal, on awakening from the chloroform, withdraws into its nest, where it remains for a few hours in a state of listlessness, probably due to the anæsthetic. It makes

its usual journeys to its food, and appears in a fair way to recovery, when, after the lapse of five or six hours, there commences a condition, well described by Koch, and characteristic of blood-poisoning. It leaves its nest, sits in the open air in a corner of its cage, its hair is disordered, its eyes glued together, it neither eats nor drinks, nor does it attend to sounds or impressions that used formerly to attract or terrify it.

This condition may end in several ways. It frequently occurs that at the site of injection, at the end of a day or two, a hard thickening is felt, extending and becoming more elevated, until fluctuation can be detected at its centre, and the process results in the formation of an acute abscess. When this occurs the general symptoms become less severe in proportion as the local symptoms grow more marked, so that, by the end of five or seven days, the former have generally disappeared, and the animal is again eating, and as lively and active as ever, although it bears on its body a small well-marked abscess at the spot where the micrococci had been injected.

If the animal be killed during the first few days, when the general symptoms are well-marked, there is found locally a red knot with a yellowish spot in its centre, and when the knot is bisected the hard red circumference and yellow centre present a picture very like that which we observe during the spreading of a soft chancre. The centre seems to be softening or liquefying into purulent matter, and the margin is thick and infiltrated around the liquefying edge. A cross section of the edge shows the presence there of dense clouds of micrococci, which, when the ordinary grouped form of coccus (staphylococcus) has been injected, are working their work of invasion in rounded masses, like clouds of dense smoke, that can when properly tinted be seen to be swallowing up the tissues by uniform peripheral invasion, the tissues a little way beyond them being rendered waxy and homogeneous, so that cell, nucleus, and intercellular substance are no longer so distinct as usual; and this halo of altered tissue apparently the result of the irritant caustic products of growth acts as an advanced guard to the clouds of staphylococci that follow and destroy all semblance of structure in the tissues, ere the latter finally deliquesce in their rear into a purulent fluid.

If the coccus injected has been the chain form (streptococcus) the process is a little different. There is a similar central breaking down into pus, perhaps not so rapid in its advance, and hence, resembling less the destructive work seen in a soft chancre; there is a like waxiness of the tissues invaded, but the invasion is not by dense clouds that destroy all trace of structure, but by the insinuation among the tissues of chains of cocci that pervade the intercellular substance and cells, forming a network of lines, between which may be seen the nuclei of the tissues. The invasion is more like the enamel on "crackle ware" china, present everywhere, yet permitting the pattern of the tissues to remain distinct.

At some distance around these foci of micrococcus growth the tissues are at first little altered, but as time goes on they show more and more condensation and thickening, the elongated cells tend to become round and the fibrous intercellular substance gelatinous, the tissues pass in fact into embryonic connective tissue or granulation tissue, and a layer of this comes in time to surround the knot.

Before it has formed the animal suffers from septicæmic symptoms, and in its blood everywhere, usually to be found without much difficulty, and in nearly every slide of blood, exist numbers of micrococci, single, in pairs, or in a small group or short chain of three or four, floating in the serum of the blood, and presenting no special affinity for the blood globules, either red or white. Now and then a group of micrococci of not inconsiderable size, containing as many as perhaps fifty individuals, is to be met with, but this is rare. I have seen it only once.

The eyelids furnish during this stage a purulent discharge containing micro-organisms, and among them numerous micrococci.

As the granulation wall around the abscess (which is evidently a reactive process by which nature, in a strong animal, limits what would otherwise be an indefinite disease) begins to form, the general symptoms tend to subside, as if it impeded the passage into the system of the micro-organisms and their ptomaïnes. When once the wall is strong and thick, the entrance of the micrococci is arrested, the abscess is as it were

sequestrated from the system, the septicæmic symptoms disappear as already described, and the occurrence of a micro-organism in the blood becomes a matter of greater and greater rarity.

But it does not invariably occur that *abscess* results. In some animals that seem to possess unusual immunity or powers of resistance, or where the dose has been a small one, the blood-poisoning symptoms begin to pass off in a day or two, and the local induration and infiltration never reach the stage of suppuration, but fade and disappear, ending in *resolution* without any further evil occurring. In some cases, on the other hand, where the reverse conditions of susceptibility or dose obtain, more severe effects are produced, as will be afterwards explained.

It will be seen, in the former report, that no such results follow the use of chronic pus, which contains no organisms, nor of pus where these have been destroyed by heat or carbolic acid; while on the other hand the micrococci, if removed from the pus and suitably cultivated, produce the same results.

This process of acute suppurative inflammation or phlegmon finds many an identity in man. Without dwelling on such a disease as soft chancre, which is an ulcer full of micrococci and other germs, but whose specific organism must be cultivated under conditions so peculiar that the disease deserves a separate description and a separate study, we find in such illnesses as poisoned wounds of the fingers and hands, so common among the working classes, in whitlows, quinsies, mammary abscesses, and common acute abscesses generally, a state of matters exactly corresponding, save that we have to hazard a guess as to the method of inoculation, being unable to demonstrate its when and how. In poisoned wounds of the hands and in quinsies, where the inflamed part communicates directly with surfaces abounding in germs of many forms, we can always suppose, and in many cases more than suppose, the introduction through a breach of surface of some extraneous matter that may convey the micrococci.[1]

[1] It is readily conceivable that in some phlegmons, such as quinsies, a rheumatic or gouty diathesis may primarily cause the inflammation, which micrococci, when ingrafted, may drive on to suppuration. Here the diathesis is the first cause, and the micrococcus the cause of its terminating in suppuration. Micrococci may modify a process begun by another cause, but they also cause inflammation without requiring such process to pre-exist.

We can also, in deeper lying whitlows about the fingers and palm of the hand, arising as they do not in the tendinous sheaths, but in the lymphatics that course in front of them in their passage between the cutaneous lymph spaces and the absorbent system of the arm, infer from their situation and connection with the absorbent system their causation from a surface breach or surface infection that may have been overlooked, or have been so slight as to be undiscoverable. Mammary abscesses and acute pelvic abscesses can be traced to the existence of the puerperal condition, and the favouring source of infection in the uterine and vaginal discharges of childbed that render frequent, at the same epoch, various other diseases whose septicæmic relations are more generally recognised. Common acute abscesses elsewhere can with wonderful frequency be traced to some local source of septicity, or to some disease more or less connected with blood-poisoning, or favouring the circulation of dangerous organisms in the system, such as fevers of various sorts, diphtheria, erysipelas, or ulcerative processes about lungs, bowels, or other viscera.

But if it be difficult to trace the precise mode of inoculation in each individual case, the demonstration of their connection with micrococci offers but little difficulty in their later stages. In each pustule or abscess the evacuation of the liquid enables us, with unfailing certainty, to recognise the presence in it of immense numbers of these bodies, amounting to hundreds of thousands or even millions in each drop, and where it is possible at the same time to scrape away a little tissue from the walls, we find in the early stages the same rich invasion of micrococcus as was described in connection with animals. We have also evidence of their passing into the system, for in many instances, especially about the upper extremity, we can observe, in the implication of the absorbents, in the lymphangitis or lymphadenitis, the inflammatory reaction that shows the absorption of some irritating matters, probably both ptomaïnes that irritate the walls of the vessels they pass through and micrococci which traverse without lodging in the vessels to be retained in the first lymphatic gland they meet with, where they are filtered out of the blood, and develope to an extent dependent on their virulence and the susceptibility of the individual. When their

growth in the lymph gland goes on to the extent of suppuration, we are in a position to verify their having passed from the original focus into it, by their occurrence in large numbers in the pus which is removed from it.

It often occurs that the process extends no further, that the lymph gland seems to be the limit of the extent to which the disease penetrates the individual, as if the ptomaïnes and micrococci passed no further, or only in so dilute a form that they neither cause general disturbances nor can be demonstrated in the blood. But this is by no means always the case. It often happens that sufficient of the germs and their products pass the lymph barrier to give rise to ptomaïne-poisoning of the whole system, revealed by fever, shivering, rise of temperature and other general disorders, while the micrococci can be found in the blood by examination of a series of slides prepared from it, numerous enough to enable us to investigate a sufficient quantity. Where the fever runs high and the symptoms indicate that absorption is abundant, every slide of blood may prove the presence of micrococci, while in less severe cases several slides, four or six, or it may be ten or twelve, may be gone through ere a micrococcus is found. With diminution of intensity their demonstration becomes more difficult, until in the mildest cases it is well-nigh an impossibility. The number of micrococci in the general circulation is in proportion to the severity of the disease. So also the numbers of micrococci in the pus are in proportion to the virulence and intensity of the inflammation. In acute abscesses of the connective tissues, we are less in a position to trace the exact course by which the micrococci and their ptomaïnes enter the system generally; but we observe the same fever and general symptoms due to their presence, and they are also to be found present in the blood in a proportion that corresponds accurately enough with the evidences of their generalisation that we can obtain from the signs at our disposal.

The completion of a well-formed demarcating wall of granulation tissue around the abscess coincides as a rule with the disappearance of the general symptoms in the individual and of demonstrable micro-organisms in the blood. Both in man and in animals the production of this wall puts an end to the pro-

gress of the local invasion. The interior of the wall of a ripe abscess presents no clouds of invading cocci, but shows only a few, and these growing but feebly among the cells on the innermost layer of the wall. Their race is run so far as that locality is concerned, and even among the pus of the cavity they no longer multiply with their pristine energy, but become more and more diluted by the liquid that collects under the influence of the tension in the cavity, so that their numbers lessen considerably in relation to the quantity of liquid. The streptococcus, under these circumstances, runs a course similar to the staphylococcus, save that in ripe abscesses due to the former there are frequently found chains truly enormous in length, where the individuals can be counted by several hundreds in a row.

There is another quarter whence we obtain evidence that micrococci are circulating in the system in these cases, and that is from examination of the urine. Normal urine contains no organisms, but in the feverish conditions resulting from phlegmons the urine frequently presents micrococci, often along with bacilli, in masses and groups, indicative of their having grown after escaping from the kidney.

Acute Suppurative Catarrh.

It is not so easy to demonstrate the casual connection between catarrhs and micro-organisms, as they necessarily occur in situations where communication with the surface of the body is free, and where therefore organisms *may* normally be found. But in every such catarrh, as gonorrhœa and purulent ophthalmia, the discharge is very rich in various forms of micro-organisms, far richer than could possibly be supposed to be the case had they no connection with the disease, and among these organisms micrococcus holds an important place. It is very abundant from the beginning, and as the disease diminishes in intensity, and the other forms become less copious among the discharge, the epithelial scales that are cast off are inhabited by large numbers of micrococci, as if the disease had been caused by their spreading among the cells forming the lining of the canal. When the disease approaches cure, the inhabited cells diminish in number, but they, as well as micrococci free among

the discharge, persist until the end, and disappear only with complete cure.

I have no experiences to detail regarding purulent catarrhs induced and studied in animals. All the observations made were in man, and these have resulted in the belief that they are due to a superficial dermatitis, of the nature of catarrh of the epithelial layer, from a growth in that layer of micro-organisms, in all probability micrococci. I have made no observations on the blood in these cases, and cannot tell whether it usually contains micro-organisms.

Sloughing Inflammation or Inflammatory Mortification.

Necrosis of the soft parts from acute inflammation can be induced in animals, and offers an excellent illustration of a disease standing midway between septicæmia and acute inflammation, presenting the features of both.

Owing to the micrococcus in human diseases being less potent in the lower animals than in man, it is not easy, as in abscess, to produce necrosis at will, but it now and then occurs, especially in mice, that among a series of inoculations, either from peculiarities of the animals or the poison introduced, a good example of inflammatory necrosis of the tissues is obtained for study.

In these cases, when a minim or two of pus has been injected, there occurs, instead of the infiltration ending in abscess, a more intense inflammatory process in which the tissues are so damaged in their vitality that they necrose almost at once, and ere they have had time to show the usual phenomena of inflammation and abscess formation. The sloughing occurs within the first two or three days, during which time the animal has shown the usual signs of septicæmia, and its blood presents, if examined, the usual admixture of micrococci. If the necrosed tissues be examined they are found full of stripes, bands, and larger masses of staphylococci, that occupy the soft parts, pervade them everywhere, and seem to affect mostly the connective tissues of the part, although they may also be seen in the lymphatic spaces, forming large spongy tufts in the midst of the coagula by which these vessels are obstructed. But the type of the disease, in the specimens I have examined, has been a *dense*

infiltration of the tissues by the staphylococcus in bands and masses resembling somewhat densely veined marble or the clouds in a windy sky.

Animals rarely die with this form, owing, I presume, to their natural resistance to the organism that produces it, so that it has occurred to me to study its fatal issue only in man. In mice the disease generally terminates in a limitation of the sloughing process within the first five days, and in a rapid separation of the necrosed tissues, with disappearance of the general septic condition. The necrosis affects only limited portions, patches of skin and subcutaneous tissue, and does not penetrate deeply, or affect entire limbs. So soon as the necrosis limits itself, the surrounding tissues exert themselves to isolate it by the formation of a wall of granulations, which bring about its detachment, and act, as formerly described, as a hindrance to the passage of the ptomaïnes or of individual cocci into the system at large, so that the animal soon ceases to present evidence of either of these occurring, and is afebrile and healthy by the time the slough has separated. The ulcer remaining at the spot is speedily filled up by granulation and cicatrisation.

It is in man that this disease is oftenest seen in full perfection, and it presents the following picture in a more or less intense degree. Starting from some cut or scratch that is generally to be distinctly made out, and affecting usually an upper extremity, a spreading inflammation, in which the surface dermatitis is the most evident, but where the deeper parts are also swelled and phlegmonous, so that the disease possesses a certain likeness to erysipelas, extends from its point of origin among the soft parts, binding them into a swollen and brawny mass, over which the epidermis is tight and glistening, or even blistered here and there from tension, showing a series of smallish vesicles. These, at first discrete, speedily flow together into larger patches. Though in less intense forms vesication may not occur, the subsequent desquamation shows that the epidermis has sympathised with the inflammation.

The pain, burning in its nature, at first local, but rapidly extending, and the elevated temperature of the part, raise in the minds of even the laity the suspicion of a poisonous matter having found its way into the limb; and this is heightened by

the involvement of the lymphatic system, shown by pain, tenderness, enlargement and induration in the cubital gland or the absorbent glands of the axilla, accompanied occasionally, but by no means frequently, with tenderness and induration, or even redness, along the line of the lymphatic vessels leading to them.

The penetration of ptomaïnes into the general system is shown by the vomiting, malaise, and feverishness that are usually present at an early stage.

The process does not present the raised edge of erysipelas.

As the disease advances, œdematous swelling precedes it in its advance up the arm, and before the elbow is reached the parts of the hand earliest invaded have gone on to abscess in the milder, and gangrene (necrosis) in the severer forms.

When necrosis results, it affects entire fingers or the whole hand, which become purple and finally black in colour, the general condition becoming greatly aggravated, with anorexia, foul tongue, sweating, flushed face, hot skin, and symptoms of collapse, the intellect remaining clear until the end.

Should death not occur, extensive suppuration in the limb, with separation of sloughs of the connective structures and of the necrosed fingers or hand, follows; and it is not unusual for the lymphatic glands of axilla or arm to suppurate as well.

Microscopically, this disease is identical with the necrosis just described in animals. The soft parts are invaded with bands and colonies of the staphylococcus scattered everywhere among the connective structures, so as to resemble the markings on marble or on pitch-pine wood. The fluids in the vesicles if opened at an early stage, show no micrococci; they are due to mere tension; but later on they, as in all the liquids of the part, present themselves in great abundance.

The blood of the body shows micrococci isolated, paired, or in very small clusters, and the number found is fairly proportionate to the intensity of the disease. In mild attacks they may be so few as to be discovered with difficulty, but they are easily found where it is severe; and in the urine they are usually present, along with a few other organisms, such as bacteria and bacilli, where the general symptoms are at all pronounced.

This disease, whose dependence on micrococcus poisoning can be followed and demonstrated on parts removed during life as

well as after death, offers one of the best instances I know of the difficulty, or even impossibility, of demonstrating its cause by the older and less perfect methods. By dry lenses and water-immersions I have sometimes observed nothing, in the sections of the soft parts, that could account for its existence. Even by the application of Koch's processes, viz., the methyl-aniline staining, the oil-immersion lenses, and the Abbé's illumination, it has often chanced that nothing was at first seen in the soft parts; so that more than once the investigation was about to be given over in despair, when the use of some other staining, notably of the aniline Bismarck-brown, has revealed the most exquisite and universal groups of staphylococci, as unlike any other structures as could well be conceived, pervading the flesh like mathematically-arrayed fish-roe or the cells of a honey-comb.

The older methods gave negative or contradictory results, while Koch's processes have always *eventually* yielded ample proof. As far as I have tried Weigert's gentian violet in this disease, it has never failed to give brilliant results.

In this disease the tendency to localisation of micrococcus is a marked feature. Although they exist everywhere in the tissues, they are seen only in close-packed colonies separated by intervals of uninvaded tissue, cohering into colonies with great tenacity. They do not transude into the serum of the blisters until a comparatively late stage has been reached, and their behaviour produces the strong belief that, though they poison the system, they do so far more by sending their ptomaïnes profusely into it, than by infecting it by detached members of their community. Septicæmia, as we are wont to call it, is present, but it is plainly more a process of ptomaïne-poisoning than a growth of micro-organisms in the blood.

Erysipelatoid Disease.

Under all forms of wound treatment there appear slight and evanescent forms of erysipelas, concerning which we are in doubt whether they are the same disease as the typical erysipelas migrans of the head and face. They commence with chills or rigors, generally associated with vomiting, and the absorbent

glands into which the lymphatics of the invaded part drain are swelled and tender. They often want the spreading margin, and are so evanescent that it rarely happens that the term *migrans* can with propriety be given them. I have had no adequate opportunity of investigating the pathology of these forms, my observations having been mostly made on a more serious form which, for distinction, I shall call *Erysipelatoid Wound Gangrene*, using the word gangrene as if it were synonymous with necrosis.

It sometimes chances that, in an individual whose constitution has been enfeebled by organic disease or prolonged suppuration, there occurs, around a wound accidentally received or resulting from some operation, a low septic inflammation, unmarked by much pain or heat, the foulness of the wound, the white painless œdema in its neighbourhood, the feeble pulse, the failing appetite, and the rise of temperature, chiefly calling our attention to the process that is present. The appetite and digestion are more enfeebled than impaired; the tongue, although white, is not foul; and the intellect is entirely unaffected.

Around the wound appears a redness—I had almost said a blush of redness, but it is no blush but rather brick-dust red—which extends for a considerable distance into the œdematous neighbourhood, and is marbled and mottled so that bands of pale brick-red colour embrace islands of white. The disease has no distinct edge, but presents itself in the form of patches of the size of the palm of the hand or less, which here and there, becoming livid or violet in hue, with detached epidermis and flaccid blisters containing bloody fluid, show the commencement of gangrene. That this disease is erysipelatoid in its nature cannot be doubted; the dirty wound with its gruelly discharge, the mottled red invasion of the living skin causing œdema in it and the subcutaneous tissue, spreading insidiously where life is, yet surely presaging the death of the parts it affects, mark a disease that the experienced eye finds no difficulty in recognising as related to erysipelas. It runs its stealthy course so secretly that patches of evident gangrene surprise one unexpectedly every here and there.

This disease, not uncommon in bad compound fractures, is, I believe, the most virulent and characteristic form of *poisoning*

by streptococcus. Although I have not had enough erysipelas material at my disposal to enable me to speak with confidence, yet I am inclined to the belief that it will be found that erysipelas and erysipelatoid diseases are all due to *streptococcus*, never to staphylococcus; and that this that has just been described, the most intense and fatal form of erysipelas, is a type of the whole class.

On examining the pus or grumous discharge that escapes from the wound, it is found to be extremely rich in various forms of micro-organisms, but especially to present the streptococcus in unusual profusion. In most wound-discharges streptococcus is by no means a prominent object, is indeed seldom present, but here it strikes the eye at once, chains of two to ten links lying everywhere scattered about in active growth, as their divisions testify.

In the skin and subcutaneous tissue around the wound, wherever the mottled redness exists, the microscopical appearances differ greatly from those described under the last disease. The tissues are not pervaded with the same clouds of micrococcus. Patches of tissue where cocci are proliferating occur only here and there, and have to be sought out with some care. Where they do exist they do not present the marbled bands and patches of the last disease, but fields of tissue with cells and nuclei comparatively little altered, show chains and clusters of the *chain coccus* insinuating themselves among the crevices, winding here and there, and tending little to form groups, giving to the tissues the appearance of being pervaded by fine thread-like necklaces of the micro-organism.

In the blood-vessels of the part there are occasionally to be found, generally in connection with the *tunica intima*, a few groups of the chain coccus; but as a rule the *blood-vessels are exempt* from serious participation in the disease. *This, on the contrary, centres in the lymphatic vessels* of the part. Every one of these is choked by a firm thrombus formed of fibrinous material with fibres interlacing in all directions, and containing entangled leucocytes; while the clot, that in the process of preparing the sections, has been so acted on by the reagents as to have shrunk and become detached from the vessel's wall, is pervaded with immense groups, chains, and masses of the strepto-

coccus, most abundant on its surface. Where a transverse section of a lymphatic vessel occurs it is seen that the cocci, though growing in all parts of the lymphatic clot, are chiefly on its outer layer and on the inner surface of the vessel, as if they had crept along the tunica intima of the latter, like the incrustations in a water-pipe, forming a tubular lining, and eventually obturating the vessel by means of a coagulum growing from the parietes to the centre of the vessel's lumen.

There exists, in fact, wherever the erysipelatous process occurs, a capillary lymphangitis of the part, leading to obliteration of all the lymph-passages by their being choked with coagula, and causing the death of the part by obstruction to its lymph circulation, as well as by the irritation of the poisonous ptomaïnes generated during the growth of the organism.

In the blood of these patients there are cocci to be found, fairly proportionate in number to the severity of the disease, and in the urine cocci, as well as rod-shaped micro-organisms, are usually readily detectable.

I have never been able to porduce this disease in animals, save by the use of the discharges collected from such a case. These, however, are so virulent that there is no difficulty in producing, by injecting them under the skin, characteristic local infiltrations and general disease. Around the injection site, in patches partly œdematous, partly red and dense, partly suppurating and cheesy, the tissues are pervaded with multitudinous chains of the streptococcus, growing in the tissues and lymphatics. The blood of the animal shows a few micro-organisms, and in one case immense balls of streptococci mixed with bacilli were found among the bile in the gall-bladder. If the animal survive the first week, and, as not unfrequently happens, tend towards recovery, the blood ceases to present any micro-organisms, even though these can still be found in plenty in the infiltrated and suppurating regions around the injection site.

One feature of this disease, as it occurs in man, viz., the yellow or earthy colour of the skin, will be treated of more fully further on.

I have been guided to the conclusion that this form of disease is characteristic of poisoning by the streptococcus or chain

coccus, while that last described is typical of poisoning by the staphylococcus or grouped organism. In the former report I left unanswered the question as to whether these two organisms were different or identical. The observations that have been made since it was written have inclined me to the belief that they are separate and distinct forms. They are often found together in abscesses, and it is then impossible to gain much information regarding them, since both possess the power of causing inflammation ending in suppuration, and both cause phlegmons. But the more disease approaches the erysipelatous type and concentrates itself in the lymphatics, the more evident does its connection with the streptococcus become, while suppurative inflammation expending itself on the tissues rather than on the lymphatics seems to be the characteristic result of the staphylococcus. To put it shortly, localised phlegmon is usually due to staphylococcus, an erysipelatoid process to streptococcus. The two diseases are in many instances not very unlike to one another, but there really exists a difference between the effects of the organisms, although by no means a great or essential one.

Septicæmia, Pyæmia, and Septico-Pyæmia, as Symptoms of Micrococcus Poisoning.

These are names directly suggestive of the idea that the disease for which they stand presents as one of its most marked features a condition in which the blood is adulterated or rendered impure by the presence in it of some morbid materials of a septic nature, and possessing some affinity with the unhealthy matters that exist in pus. The basis of truth that underlies this supposition has, however, gradually been brought to support a hypothesis that in the disease the entity *blood-poïsoning* is fundamental and essential; that in an infective matter entering the blood and developing chiefly there, as yeast develops in a suitable liquid, is to be sought the key to a knowledge of the malady.

It has been sufficiently stated above that such a hypothesis finds no support either in a study of analogous conditions of the system or in such facts as can be made out by combined clinical and pathological observations on the disease itself.

It has been shown that the characteristic phenomena of ordinary zymotic diseases are inexplicable on the supposition of

the morbid cause having its citadel in the blood, but can be readily understood if the tissues be the entrenchments which they occupy, and the blood merely a province where a guerilla warfare is carried on.

In gradually presenting the various forms of micrococcus-poisoning in increasingly malignant phases, and noting how each presents, along with its local phenomena, the signs of a concomitant blood-poisoning that likewise rises in the scale of malignancy until it presents all the features of well-characterised septico-pyæmia, I have endeavoured to pave the way for the disease whose titles head this chapter being considered as merely part of a disease, sometimes the only part evident to our unaided senses, but in reality a subordinate part of a real disease that is somewhere raging in a local centre, could we but discover it. In this chapter I shall strive to show that not only occasionally or frequently is septico-pyæmia the companion of a local disease, but that it invariably is so, and should indeed be considered as the shadow of a disease whose substance is to be found in the tissues, without which it could have no existence.

In the ground already traversed it has been maintained that associated with all local acute suppurative inflammations there exists a feverish condition due to a slight form of septicæmia from passage of organisms and ptomaïnes into the blood, or in other words, that inflammatory fever is a mild form of septico-pyæmia. It has also been urged that in phlegmonous diseases, severe from the outset, or that have passed from a mild beginning into a severe after-stage, the inflammatory fever becomes more intense, presents the ordinary picture of septico-pyæmia. And the next point in the natural sequence of thought is to discuss the conditions where the disease presents so much of the general and so little of the local character as to have given rise to the assumption that the latter did not exist.

But, prior to doing so, I would wish to draw attention to a class of cases that do not belong either to what is ordinarily understood as acute suppurative inflammations on the one hand, or septico-pyæmia on the other, and which yet throw much light on both. The disease called *malignant lip pustule*, generally looked upon as a malady *sui generis*, is an instance of a highly fatal disease where a local focus presenting at first the pheno-

mena of inflammation hurries rapidly on to the stage of suppurative infiltration or gangrene, while coincidently there occurs a general condition of blood-poisoning that tends to prove rapidly fatal. The local centre of disease, like an ordinary acute inflammation, is at first taken for nothing more, but combines a rapid unfolding of local virulence, evidenced by its quick extension into the healthy neighbourhood, and the rapidity of its passage through the ordinary stages of inflammation to terminate in slough or suppuration, with the development of general symptoms indicative of a serious poisoning of the system.

It seems as if some toxic agency akin to that of typhus and typhoid fevers were at work, and rapidly led to the production of a *typhoid* state, where high fever and disorders of the nerve centres created the most imminent danger to the life of the individual. Malignant lip pustule occupies a highly vascular site, whence rapid penetration into the system is greatly favoured. It indeed has all the outward character of a *phlegmon*, with in addition grave general symptoms, and its names all point to this resemblance (carbuncle anthrax). Nor is this to be wondered at, for it is in all probability nothing more than a virulent phlegmon in a vascular region, and occurring in a subject of low vitality and diminished resistancy. In the one case, where I had occasion to examine the disease, it occurred in a male aged forty-five, a patient of Dr. Trail of Strichen. It consisted of a spongy purulent infiltration of the whole thickness and length of the lower lip for a full finger's breadth from the margin downwards. The general symptoms were most alarming, the patient's life was in serious danger when I saw him, on the eighth day of the disease. The lip was pervaded with innumerable sloughs and miliary abscesses, and these crowned with groups of staphylococci, each coccus averaging $\frac{1}{1480}$ of a millimetre in diameter. There were no streptococci present. The pus was estimated to contain 90,000 cocci in each cubic millimetre. One half minim injected under the dorsal skin of a large mouse killed it in forty-eight hours, with the usual symptoms of septicæmia, and the œdematous injection site showed one gigantic colony of grouped coccus not yet reaching the stage of suppuration, while the blood contained similar cocci in less abundance. The blood from the heart was unable to

produce any infection when rubbed into shallow scratches on the ear of a stout guinea-pig. The patient eventually recovered by thoroughly drenching the tissues of the lip with carbolic acid solution slowly injected into it through numerous punctures while he was under the influence of chloroform. In my judgment, this man's disease was a very virulent staphylococcus colonisation in a vascular region, where, either owing to defective resisting powers or to extreme virulence of the micro-organism, there was little attempt at limitation of the process by granulation tissue being formed around it, and hence the system was poisoned, more however by the ptomaïnes passing into it than by the individual cocci that strayed into the blood. These latter seemed to have found the blood unsuitable for their existence, as was shown by the absence of any secondary foci in any other part.

Acute infectious osteomyelitis is another disease where septicæmia exists along with a well-marked local centre whence it springs. Of this disease I have seen but one example of late, and it occurred in the practice of Dr. Williams of Tarland. A young boy, naturally delicate, and who had been exposing himself for hours to the intense cold of the winter of 1880–81, was taken with rigors and pains in his right tibia and left ribs, rapidly developing into a well-marked acute inflammation of the medulla of the tibia. The symptoms over the tibia were heat, slight redness, great swelling, and intense pain; the ribs presented a similar affection complicated with pleuro-pneumonia, and the general symptoms were of the severest typhoid type, with high fever, ending in stupor and death. When an incision was made over the lower part of the tibia, where the greatest pain was complained of, and a drill sent through the compact layers of the bone, the usual oily pus of osteomyelitis squirted out, showing the great pressure it had been subjected to, and was found to contain large numbers of the staphylococcus. The evacuation of the pus was not followed by much improvement in the general symptoms, although it relieved the local pain. It was unfortunately not in my power to obtain any of this pus for an experimental investigation. The facts of the case suggested the following explanation. This boy, constitutionally feeble, chilled by long periods of exposure to the intense frost, had the

forces of his tissues so weakened that invasion of micro-organisms from without or from the intestinal tract had occurred in his system. Of these organisms the staphylococcus, developing in his weakened frame, had found a suitable resting-place in the medulla of his ribs and tibia. There it had developed into colonies, that produced their usual effect, viz., acute inflammation, and from thence the ptomaïne-poisoning had occurred that eventually caused his death.

These two diseases will serve as types where we can see septicæmia and pyæmia, in undeniable clearness and purity, yet dependent upon a local disease that cannot be explained away as being other than their true cause and starting-point, and will illustrate the questions that confront us in dealing with septico-pyæmia.

There is no such disease as septicæmia or pyæmia *per se*, such conditions are merely secondary in the order of the morbid process and depend on the existence of local foci of micrococcus growth. They are but the expressions of malign influences coming from this focus, and would in every case cease to exist were it in our power to remove or cure the focus. From text-books and monographs, not from nature, we have learned to believe in them as possessing an individual existence. But is this correct? There is no observer, accustomed to observe with care and ponder with earnestness, and whose pathological knowledge has kept pace with his clinical study, who will be able to assert that he has seen a case of septicæmia existing alone. I have never personally met with such. In the work of the surgical wards, as in the more varied experiences of general practice, it has always been the reverse: individuals who have been injured or operated on, or who have become the subjects of acute inflammation or gangrene, or who have presented some lesion or wound whence the process had originated, have been the only ones who have exhibited septicæmia or pyæmia. And wherever there has appeared an acutely inflammatory disease, whether arising by seeming spontaneity or beginning in a wound, there, so surely as the signs of general invasion were present and the thermometer in the axilla showed a temperature considerably exceeding 101° Fahr., did the microscope reveal in the local discharge the existence of micrococcus, and its presence

to a less extent in the blood. If the patient grew worse, then the local discharges showed a greater abundance of the cocci, and the blood became more pervaded with them, the intensity of the local inflammation and of the general signs corresponding with the numbers of these organisms present, and the signs of their active growth as shown in their rapid division. Did the patient tend towards recovery, the fact was signalised by a diminution in their number, as well as by the favourable conditions of pulse, temperature, and functions that are familiar to us all.

It will occasionally happen that the general symptoms are very marked, while the local disease may be hard to discover. Not every large colony of micrococcus signalises its presence by the clamant signs of redness, heat, pain, and swelling; on the contrary, where the tissues or the individual affected are weak, the growth and invasion may proceed with such astounding celerity that large tracts are invaded and the system is saturated with the ptomaïnes ere we are well aware that anything is going wrong. Even then, care will detect the local site of infection. Experiment on animals shows that if micrococci that have been cultivated into great virulence, such as those taken from a virulent suppuration, or, as stated above, from a malignant phlegmon, be injected, especially into a weakly animal, it exhibits a disease that looks like septicæmia; it fevers, its nerve centres become intoxicated, it is dull and listless, and in a few hours it dies; everything pointing to the ailment of which it perishes being generalised in its system, while at the injection site a little puffiness may be all we discover. Yet when the animal is subjected to microscopic scrutiny, we find in the seemingly unimportant injection site an enormous and appalling growth of the deadly organism, in quantities that defy calculation, in numbers that would be but faintly computed by millions, while the blood which we would naturally have supposed to be richly inhabited, is so poorly provided with the organisms that it is clear that the chemical intoxication by the ptomaïne, not the vital injection by the germ, has been the cause of death. The local invasion has been so swift that the symptoms betraying it have been but few. In my former report I have mentioned the case of a man where septicæmia followed

an extirpation of goître, as well as a case of compound dislocation and fracture where the microscopic investigation was full and convincing, and I have other cases since that report was written that tell the same story.

Where cases of septicæmia end, not in death but in recovery, the part played by the local focus usually becomes evident, for suppuration and inflammation, it may be gangrene and necrosis, arise in and around it, so that the poisonous centre that may once have presented so few symptoms is made plain, and health is not regained until it is extruded by the agencies of reaction and repair.

It cannot be needful that all the gradations between the most intense forms of disease where the general symptoms are striking and the local ones obscure, and the slightest forms where the local symptoms are patent and the general almost or altogether undistinguishable, be again commented upon in detail. The matters previously gone over are sufficiently illustrative, and I may now simply refer to these as warranting us in concluding that phlegmon and septicæmia are but one disease, produced by micrococcus poisoning in some of its varying degrees of intensity. To use the language of Kocher, "between a simple localised acute inflammation on the one hand, and the severest case of pyæmia, there exists only a difference in degree, a difference in intensity."[1]

Phlegmonous inflammation, septicæmia, pyæmia, and septico-pyæmia are all micrococcus poisoning, varied, however, according as ptomaïne intoxication or the local tissue reaction becomes more prominent. Every feverishness, from an inflamed throat or finger, is a septicæmia in a mild degree, and may pass into a severe form. Ptomaïnes pass into the blood, and coincidently a few individuals of the micrococcus may be found to have wandered from the local disease and to be circulating in the blood, dead or half-dead, owing to the unsuitability of the medium where they are and the unfavourable influences of the forces of the tissues. If removed from the blood they rarely grow when put into a suitable medium. They are all eventually extruded or consumed. But if the individual be subjected to

[1] Kocher, "Aetiologie der Acuten Entzündungen," Langenbeck's *Archiv*, vol. xxiii. p. 103, 1879.

depressing influences, the ptomaïne poisoning may not be the only phenomenon observed. As the symptoms become more severe and the micrococci more numerous in the blood, the weakness of the individual becomes greater and the resisting power of his tissues less, so that the micrococci are able to live in the blood, where previously they found this impossible. They multiply and form small groups that increase in size until they are too large to pass through the capillary network, and therefore are caught and detained in lungs, liver, or some other part. There they continue to increase during life, perhaps even for a time after death, and furnish their contribution of poison to the system.

Or it may be that, though unable to multiply in the blood, they here and there throughout the body find spots suitable for their development, where they can multiply and form the foci of suppuration that mark the form for which we usually reserve the name *pyæmia*. The pyæmic secondary foci are usually in lung or liver, or joint, but may equally well occur in lymphatic glands, secreting glands, or even in connective tissues. They are but a rehearsal of the local growth and infiltration already described in the primary focus, and require no separate description. In the joint affections of pyæmia, however, there has seemed to me to be something peculiar. It would naturally be imagined that the organisms in the blood, finding their way into the quiet haven afforded by the joint cavity with its tranquil pool of synovia, would multiply in that liquid until they and their ptomaïnes were sufficiently numerous and intense to provoke reaction, when the phenomena of arthritis might be expected to appear. But this does not seem to be their course. In one pyæmic case, when I drew off by the aspirator a little serum from a knee-joint at an early stage of the disease, there were no micro-organisms in the fluid, and it was only at a later period, when it was becoming purulent in character, that these appeared. From this I surmised, perhaps incorrectly, that pyæmic arthritis is not due to organisms multiplying in the cavity, but somewhere in its neighbourhood, possibly in the delicate synovial fringes around the cartilages where the capillary network is very fine, and that the early liquid in the joint is merely the serum or synovia effused from the outer surface of

the spot where the colony of micrococcus is still in a comparatively unadvanced stage of growth.

There is one phenomenon common both to septicæmia and pyæmia that requires to be mentioned here, although I regret that my observations concerning it are so barren of result. I refer to the *yellow colour* of the skin observed in severe cases. This symptom has been merely mentioned in the portions of this report devoted to sloughing inflammation and erysipelatoid disease. But it is common to all severe forms of micrococcus disease. It shows itself as a paleness or earthy tint of the skin, nails, gums, and conjunctiva, that may vary in depth of colour up to a distinctly icteric tint. It differs from ordinary jaundice, however, in not affecting the urine. There is plainly some connection between this colour and micrococcus. In wounds that contain micro-organisms, and that are covered by Lister's dressings, it is very common to remark portions of the gauze tinted of a rich yellow or orange hue, and I was early led to observe that a microscopic examination of these patches never failed to reveal the presence of micrococcus. So invariable was their connection that it was evident the colour depended on the presence of micrococci. It occasionally chanced that it was observable on other dressings, or even in the pus of a wound, but wherever it was seen I have always detected large quantities of micrococci. I cannot say that the wounds where this orange colour occurred have given evidence of being more dangerous than other wounds, although it were well not to forget the statement of Verneuil,[1] that such wounds are apt to be associated with dangerous forms of blood-poisoning. The orange colour indicates the presence of micrococci, and therefore such wounds are not pure; danger lurks in them, but the regular use of antiseptics and drainage removes the danger. In cultivating micrococci the yellow tinge was sometimes obtained. This was rarely the case, and the colour was but faint in albuminous fluids exposed to the air, but in the interior of eggs it was sometimes very marked. It was not much seen when the streptococcus that rapidly and uniformly pervades the whole egg was employed; indeed the yellow tinge then seen in the albumen may have been due to the admixture of the yolk that results from the agitation of the all-pervading growth.

[1] *Archives gén. de. Med*, December 1880, p. 641, "De la Suppuration orangée."

But where the staphylococcus was employed a different style of growth and a very marked coloration was several times observed. Staphylococcus grows at the injection site, not tending to spread rapidly, but rather to mat all that lies around it into a firm turf or clod, and the resulting clot-like turf was in several instances found of the deepest orange yellow next the shell, as if the colour were the result of the growth of the organism under peculiar conditions. Hence it appears possible that the yellow or earthy tinge of the surface observable in cases of septicæmia may be in part at least due to the production of a yellow pigment by the micrococcus.

Should the views here advanced that septico-pyæmia is simply micrococcus poisoning prove to be correct, it will be necessary to go a step farther and admit that *hectic fever*, that septicæmic condition that differs from ordinary septicæmia in being associated with *ulcerative phthisical* processes in the lungs, and with ulcerative diseases in general, rather than with wounds and operative procedures, is but a form of the same disease. This I am prepared to assert. Although in the hectic of phthisis we have to deal with a milder and more protracted, although equally fatal form, yet there is no clinical difference in the appearances or symptoms from those that occur in septicæmia from advanced disease of the hip-joint or spine, or in the suppuration resulting from a bad compound fracture not treated antiseptically. The two diseases are absolutely identical, and surgical septicæmia and hectic fever are really synonymous terms. Hectic fever only occurs where there is a tendency to suppuration; it does not exist in phthisis until suppurative breaking down of the lung occurs, and micrococci are always present in the expectoration of such cases. Without septic suppuration, hectic fever never exists. In tubercular maladies there is no reason to suppose that the micrococci are other than ingrafted on the diseases when they have reached a certain stage, having been conveyed into the lungs by inspiration, or through the circulation, and similarly appearing in chronic suppurations about pelvis, spine, or joints, either by the rare penetration into them from within or the more common introduction from without. Finding in the weakened tissues a spot where their development is more or less favoured, they secure at first perhaps a scanty foothold, and commence only,

when the prostration of the individual permits their considerable extension, to show the more serious symptoms of their presence.

One of the chief difficulties in the way of admitting what is here claimed as due to micrococcus will, in all probability, be that it is not readily conceivable how one organism should produce such variety of disease. Yet a little consideration will make it plain that all the variations in the nature and symptoms of the diseases produced may be due to—1st, the difference in the form of the organism; 2nd, differences in the organ or structures invaded; 3rd, the difference in the virulence of the organism; and 4th, the different susceptibility of the individuals attacked.

1. *On the difference in the form of the organism.*—I have already dwelt on the modes of growth of the streptococcus and staphylococcus, and their correspondence with certain varieties of disease. It may be true or not that time will reveal further differences among the micrococci found in the pathological conditions; this I cannot tell. It may also well be true that there are other micro-organisms besides micrococcus that can give rise to acute inflammations and septico-pyæmic conditions; this also I cannot tell; I only know that they must be rare. Last year Professor Ewart put on record an investigation into an epidemic of sore throat, fever, and rheumatic pains, followed *in a few instances* by local suppurations, seemingly due to a rod-shaped bacillus, not a spherical coccus.[1] Febrile maladies, however, often open a door for the entrance of micrococcus, so that abscesses and inflammations due to the latter are common as sequelæ of the former, and this renders the question a hard one to decide. It is certain that septicæmia in animals is not usually due to micrococcus, but to other organisms; and these may be capable of occasionally appearing in man. But, with these reservations, I do not hesitate to say that micrococcus is the cause of all septico-pyæmia, as of all phlegmonous inflammations in man.

2. *The differences in the organ or structure* affected may well be expected to explain to a considerable extent the clinical ap-

[1] *Proceedings of Royal Society of London*, 1881, No. 215. A new form of febrile disease associated with an organism distributed with milk.

pearances seen in the diseases due to micrococci. Inflammation of a lung, a serous cavity, an eyeball, or a vein, cannot be expected to give rise to identical symptoms, and such considerations as belong to locality will explain much that would otherwise be startling in the extensive range of diseases caused by these organisms.

3. *The varying virulence of the organism* seems to play a large part in the multitude of disease-forms it originates. Micrococcus, as it exists on the surfaces of our bodies and in decomposing fluids, is a comparatively innocent germ, that may, in the state and quantity it there exhibits, be injected under our skin with impunity. I have never succeeded, I freely admit, in cultivating such cocci into the virulence sufficient to produce inflammation and disease, although I have often reduced virulent cocci into a harmless condition by growing them with free access of air. Yet, despite my failures, I believe that they are one, and that it will yet be found possible, by growing them under proper conditions, to demonstrate their identity. From the experiments mentioned in my former report, it seems probable that cultivation in animal fluids and exclusion of air are the chief conditions requisite to bring forth their virulence; while this is diminished by being grown in fluids not of an animal nature, and under free access of air. All that has been observed concerning them, experiments made with them, and their behaviour as seen in disease, seem to favour this view.

If analogy may be claimed as giving strength to such a supposition, it points entirely towards culture evolving virulence. It is now a well-worn observation that harmless organisms can be made deadly, and deadly ones harmless. Grawitz cultivated innocent fungi into virulence; and in Buchner's experiments we can see the common hay-bacillus growing into a troublesome, an alarming, a most dangerous, and lastly a certainly fatal organism, more lethal than the most subtle chemical poison. In the great facts of protective vaccine that we owe to Pasteur and others, we find the converse process laid bare to us, and can observe how, with the diminishing virulence from suitable culture, the properties of an organism become marvellously changed. Pasteur says, concerning the organism of splenic fever[1]—"The small

[1] *Comptes rendus du Congrès International des stations agronomiques*, Paris, 1881, pp. 154, 155.

filamentous organism of anthrax readily produces spores. It generally grows by dividing, like the little organism of fowl-cholera; but after twenty-four or forty-eight hours, especially if grown with abundant exposure to air, which it requires if it is to grow by fission, there appear in the slender filaments composing it small brilliant points, its spores; around these the filament becomes absorbed and soon disappears, leaving only a cloud of minute brilliant granules. This is but another mode of generation of the anthrax parasite; for if you take these brilliant grains and place them where they can grow, they immediately reproduce the filamentous organism that grows anew by fission for several days, then again forms spores, and so on. But here is a strange peculiarity: when the spore forms in the rod it possesses the exact virulence of the rod or filament; that is to say, if you cultivate the blood of an animal that has died spontaneously of anthrax till in twenty-four or forty-eight hours it forms spores, you will find, if you test the virulence of these germs, that it is identical with that of the blood from which they were produced.

"There are two circumstances under which the small filamentous organism can develop without producing spores,—a very low temperature, about 60° Fahr., and a very high one, about 110° Fahr.

"Bring the liquid where the anthrax is sown to a temperature of 104°, or perhaps 20° or 30° below that point, and it grows and forms spores; but at the temperature of 110° Fahr. it grows quite as well as at the lower temperature, only it forms no spores.

"Now leave it at this temperature, so that it is exposed at the same time to the action of the oxygen in the atmosphere of the vessel, and then do as you did in studying the organism of fowl-cholera, that is, studying the effect of time on its virulence. When you have kept the flask at 110° Fahr. for four, five, or six days, you test its virulence, and find that it already gives evident signs of diminution; in eight days this is more manifest, and in ten days, fifteen days, or a month, it becomes step by step more feeble. After a certain lapse of time it is all dead, the organism will not respond to further culture; but before it dies, if you test its virulence, you will find you can kill neither guinea-pigs,

sheep, nor rabbits; and in the interval of time that has elapsed between the exposure to the temperature of 110° Fahr. and this extreme period of a month or six weeks, you have *as many viruses differing in their virulence as you have days.*" [1]

In the face of these statements concerning one organism, it is not an extraordinary thing to assume that the same may be true of another, and that the micrococcus may vary greatly in its virulence.

4. But *the different susceptibility of the individual* probably plays the most important part in varying the forms and intensity of micrococcus poisoning. If the same dose of micrococcus pus be injected into each of a number of mice of the same litter, the effects of the dose will greatly vary—perhaps one, the largest and strongest, may escape unscathed or be but slightly ill, in several others abscesses will follow, in some necrosis, and in one perhaps, the smallest or most weakly, death from septicæmia results. Here the evidence of individual susceptibility is very strong.

When we reflect on what we know of other diseases, it becomes even stronger. In an epidemic of measles or scarlatina all are not affected alike; some are seriously ill and die, some are trivially affected, others entirely escape and will not take the disease. A family of children, constitutionally strong, takes the disease and considers it a pastime; a hundred yards off, a delicate family also takes it, and several of its members die; while a third family, naturally healthy, but living in a badly-drained house, also pays a toll of several lives.

And not only does intensity seem to be modified by constitution, but the very form of the disease can be altered by it. In typhoid fever an individual will have an attack of the disease lasting three weeks, another six weeks, a third will have no diarrhœa, a fourth will simulate acute bronchitis or acute disseminated tuberculosis, a fifth will be struck down comatose, as if from apoplexy, at the very commencement, and so on.

[1] M. Pasteur goes on to show how each of these degrees of virulence can be definitely fixed by transferring the organism to a temperature in which spores are formed, when these at once appear, possess exactly the virulence the bacilli had got to, and keep it indefinitely, so that a known degree of virulence can be sent to the ends of the earth.

Hæmorrhagic smallpox differs from common variola only in the individual constitution of its victim, and yet how unlike are the diseases. It were easy to multiply evidence of the great part played by individual constitution in modifying the forms assumed by the same bacteric diseases.

The agencies at work in modifying the intensity, situation, or extent of micrococcus poisoning are so potent, that there will be found to be nothing in the variety of its forms and stages that does not readily harmonise with the assumption of their being due to but one disease.

It is greatly to be regretted that additions to our knowledge do not immediately result in additions to our means of treatment. We are still far from possessing a cure for septic diseases. Yet there is some gain in the way of treatment to be derived from these views, should they prove to be true. We must, in the first place, abandon the idea that by the internal administration of general remedies we can eradicate from the blood or neutralise in it diseases whose essence is not to be found there, but elsewhere. We must zealously fall back on our local measures, striving to prevent the introduction of germs, and to destroy the local colonies of those that have entered. The present is an epoch when it seems somewhat unfashionable to be a thorough antiseptician in theory and practice, when such words as bacteria and carbolic acid have become commonplace and vulgar, and when there is danger of reaction carrying us back towards our old aimlessness in treatment.

Human nature forgets unseen foes, but were every surgeon and physician familiar with the microscopic study of micro-organisms, then, dealing as we would with visible realities, and beholding both our faults and their punishment, in the treatment of wounds and disease, it would be less easy for fashion to mislead or prejudice to warp our minds.